IN THE CLAIMS:

Please replace claims 150 and 159 with amended claims 150 and 159 as follows:

150. (Amended) The method of claim 138, wherein the heterologous nucleic acid molecule encodes a product that alters the organism's immune responses and the conditions comprise administering to the organism an immunosuppressive agent.

159. (Amended) The method of claim 131, wherein the organism has undergone a bone marrow or solid organ transplantation.

REMARKS

A check for the fee for a five month extension of time accompanies this response. Any fees that may be due in connection with filing this paper or with this application may be charged to Deposit Account No. 50-1213. If a Petition for Extension of time is needed, this paper is to be considered such Petition.

Claims 1-165 are presently pending in this application. Claims 150 and 159 are amended to correct errors in claim dependencies that rendered claims 150-154 duplicative with claims 145-149 and claim 159 duplicative with claim 158, as noted by the Examiner. Basis for amendment of claims 150 and 159 can be found in the claims from which they depend as amended and elsewhere in the specification such as, for example, at page 27, line 28 to page 29, line 5. No new matter is added.

A Supplemental Preliminary Amendment and Replacement Sequence Listing is also filed on the same day herewith under separate cover. The Supplemental Preliminary Amendment corrects minor typographical and formatting errors in the specification and claims, and incorporates a sequence set forth in Figure 1 of the specification into the Replacement Sequence Listing.

A sheet showing marked-up amended claims 150 and 159 pursuant to 37 C.F.R. §1.121 is attached hereto.

LACK OF ANTECEDENT BASIS

The Examiner alleges that claims 85 and 97 lack antecedent basis for "the conditions," and that the dependency of both claims must be corrected. Applicant respectfully disagrees.

It is respectfully submitted that claim 31, which recites:

> exposing the first and second cells to conditions that inhibit unaltered mammalian enzyme but to which the altered mammalian enzyme is resistant . . .

provides the antecedent basis for claims 85 and 97. Each of claims 85 and 97 ultimately depend on claim 31. Claim 85 depends on claim 33, which in turn depends on claim 32, which depends on claim 31. Claim 97 depends on claim 87, which in turn depends on claim 86, which depends on claim 31. Therefore, there is proper antecedent basis in claim 31 for claims 85 and 97 as originally filed.

TRAVERSAL OF THE RESTRICTION REQUIREMENT

The Examiner alleges that claims 1-165 can be divided into 26 patentably distinct groups. The Examiner further sets forth a Sequence Election Requirement applicable to each of the twenty-six groups. Applicant respectfully traverses the Restriction Requirement as between Groups III-XXVI, and the Sequence Election Requirement as to all twenty-six groups.

It is respectfully submitted that the Restriction Requirement as between Groups III-XXVI is improper. In order for restriction to be proper under 37 C.F.R. §§1.141 and 1.142, the restricted subject matter must be independent or distinct **AND** there must be a burden on the Office to examine the claims in the claims in the same application. In this instance, as discussed below, Applicant respectfully submits that the Office has failed to demonstrate either of these requirements.

Arguments demonstrating the impropriety of the Restriction Requirement as set forth

The test for the propriety of a Restriction Requirement is two-pronged. The first is whether the claimed subject matter is independent or distinct; and the second, is whether there is burden on the Office to examine all claims in the same application.

It is alleged that the claimed subject matter of Groups III-XXVI are distinct because each group either contains a different enzyme or requires different techniques to introduce the nucleic acid to the first cell (such as *in vitro*, *in vivo* or *ex vivo*), or the first and second cells are compared under different conditions (*in vitro* or *in vivo*) or an additional marker nucleic acid is introduced into the first cell. The Examiner alleges that the search required for any one of Groups III-XXVI is not required for all of the others because the technique used in each group is allegedly different from that in all the other groups.

It is respectfully submitted that, with respect to all Groups III-XXVI, the premise upon which the requirement is based is incorrect. Groups III-XXIII and XXVI are directed to a method of providing for selective proliferation of a first cell relative to a second cell by introducing a nucleic acid encoding an altered mammalian enzyme into the first cell that imparts resistance to conditions that inhibit viability and/or proliferation of the second cell. Groups XXIV and XXV are directed to a method of transferring a heterologous nucleic acid molecule into an organism by conferring selective proliferation and/or viability on a first cell relative to a similar second cell in the organism by introducing the heterologous nucleic acid along with a marker nucleic acid into the first cell. Such methods, while possibly containing distinct species (and, as noted, possibly two different methods), are not directed to separate and distinct subject matter.

A) Independent or distinct

1) The Restriction Requirement does not contain any Group that encompasses the generic claims as set forth herein.

As discussed above, the claims of Groups III-XXIII and XXVI are directed to a generic method of providing for selective proliferation of a first cell relative to a second cell in which a nucleic acid is introduced into the first cell such that it confers on the first cell a resistance to conditions that inhibit the growth (viability and/or proliferation) of the second cell. Similarly, the claims of Groups XXIV and XXV are directed to a generic method for transferring a heterologous nucleic acid molecule into an organism in which a first cell in the organism is subjected to selective proliferation and/or viability relative to a similar second cell in the organism by introducing the heterologous nucleic acid molecule along with a resistance-conferring marker nucleic acid into the first cell. Dependent claims specify particulars of the methods, such as the class of enzyme encoded by the nucleic acid, the specific enzyme within that class, the types of cells, or whether the selective proliferation or the introduction of the nucleic acid into cells is performed *in vivo*, *ex vivo* or *in vitro*.

Contrary to the Examiner's assertion, the claims are not directed to methods whose steps or techniques differ based on the type of enzyme encoded by the nucleic acid, nor do they differ based on whether the selective proliferation or the introduction of the nucleic acid into cells is performed *in vivo*, *ex vivo* or *in vitro*. Both sets of method claims are based on the are encompassed by the generic concept that selective proliferation of a first cell relative to a second cell can be achieved by introducing a nucleic acid into the first cell such that the nucleic acid confers resistance on the first cell to conditions to which both the first and second cells are exposed. The method claims of Groups III-XXIII and XXVI are directed to selective proliferation based on the aforementioned generic concept, and the method claims of Groups XXIV and XXV are directed to the introduction of a heterologous nucleic acid molecule into a cell and are encompassed by a generic method.

By setting up the requirement as a Restriction Requirement rather than an Election of Species, there is no group that encompasses the generic methods as set forth, *e.g.*, in claims 23 and 31, which do not specify that the nucleic acid encodes a particular enzyme (*see also* claims 24-30, 32 and 86, dependent thereon, that do not specify a particular enzyme). Not only is it not reasonable to require Applicant to obtain twenty-six patents to cover some of the subject matter claimed in the application, it is unfair to deny coverage to all of it, by setting up a Restriction Requirement that eliminates the possibility of generic ~~coverage. Therefore, the Restriction Requirement as set forth is incomplete,~~ since all claimed subject matter is not included.

2) The Restriction Requirement is improper because it does not include"linking" claims within any of the "Groups", the Requirement does not specify the "linking claims" set forth herein, nor is it conditioned on the allowability of said "linking claims."

Genus claim 23 is drawn to a generic method of selective proliferation that employs a nucleic acid encoding an altered mammalian enzyme. Claim 23 recites:

> 23. A method of providing for selective proliferation, viability or proliferation and viability of a first cell relative to a second cell, comprising:
> introducing a nucleic acid encoding an altered mammalian enzyme into the first cell; and
> exposing the first and second cells to conditions that inhibit the unaltered mammalian enzyme but to which the altered mammalian enzyme is resistant;
> whereby the first cell exhibits greater proliferation, viability or proliferation and viability relative to the second cell.

Claim 31, which is a subgenus of claim 23,differs from independent claim 23 by specifying that the nucleic acid encodes an enzyme of a nucleotide biosynthesis pathway. Claim 23 is generic to claim 31, and each of these claims link the dependent claims. Thus, Claims 23 and 31, drawn to a generic methods of selective proliferation that employ nucleic acid encoding an altered mammalian enzyme, "link" Groups III-XXI, which are restricted based on the

particular species of enzyme encoded by the nucleic acid (*see* MPEP §809.03, which defines one type of linking claim as a genus claim linking species claims).

Furthermore, with respect to Groups III-V, Groups XIX-XXI, XXII, XXIII and XXVI, each of claims 23 and 31, which are generic claims drawn to a method of selective proliferation in which a nucleic acid encoding an altered enzyme is introduced into a first cell relative to a second cell, links Groups XXII, XXIII, XXVI, Groups III-V and Groups XIX-XXI, which are restricted based on whether the nucleic acid encoding the enzyme is introduced into a cell *in vitro, ex vivo or in vivo*.

According to MPEP §809, when claims linking more than one group are found, the Restriction Requirement must be conditioned on:

1) specifying the linking claims; and

2) examining the linking claims with the elected group. The linking claims **must** be examined with the elected group; if the linking claims are deemed allowable, then the restriction requirement must be withdrawn and all claims directed to nonelected subject matter which depends from or includes all the limitations of the linking claims must be rejoined.

Therefore, the Requirement for Restriction must specify that they are linking claims, and these claims must be examined with the elected group. The Requirement for Restriction must further be conditioned on allowability of the linking claims; if the linking claims are deemed allowable, then all Groups that are linked by the linking claims must be rejoined.

The "Groups" set forth in the instant Restriction Requirement do not specify nor examine the claims 23 and 31 as generic claims. Accordingly, the Restriction Requirement as set forth is improper.

3) The Restriction Requirement could be Redrawn

Applicant respectfully submits that the Restriction Requirement could be redrawn in order to properly include the generic subject matter. It and set forth in four groups as follows:

Group 1, claims 1-6, drawn to an isolated human IMPDH protein that contains one or more alterations (former Group I);

Group 2, claims 7-22, drawn to an isolated nucleic acid encoding IMPDH that contains one or more alterations (former Group II);

Group 3, claims 23-137, 141-144 and 160-165, drawn to a method of providing for selective proliferation or an advantage thereof of a first cell relative to a second cell (former Groups III-XXIII and XXVI); and

Group 4, claims 137-140 and 145-154, drawn to a method of transferring ~~a heterologous nucleic acid molecule into an organism by selective proliferation~~ and/or viability of a first cell in the organism where the first cell contains the heterologous nucleic acid molecule introduced therein along with a marker nucleic acid, relative to a similar cell in the organism that does not contain the marker nucleic acid (former Groups XXIV and XXV).

If deemed appropriate, an Election of Species in Group 3 could be required for search purposes. It is noted, however, that Election of Species with respect to: (A) the *in vitro*, *ex vivo* or *in vivo* introduction of the nucleic acid encoding either IMPDH (Groups III-V), DHODH (Groups XIX-XXI) or other altered nucleic acid (Groups XXII-XXV) into a cell, or; (B) comparing proliferation of the first cell against the second cell either *in vitro* or *in vivo* (Groups XXII-XXV against Groups III-V; XIX-XI; or XXVI), would not be correct. Election of Species may only be required when more than one independent and distinct species are claimed or where at least one independent and distinct species is claimed together with a genus.

The Group 3 claims of the "redrawn" Restriction Requirement as set forth above contains claims directed to generic methods of providing for selective proliferation of a first cell relative to a second cell that are altered in scope in the dependent claims by specifying particular embodiments, such as comparison of proliferation of the first cell against the second cell either *in vitro* or *in vivo*; or *in vitro*, *ex vivo* or *in vivo* introduction of the nucleic acid into a cell. Under U.S.

patent practice, Applicant is entitled to claims of varying scope and is not required to claim each and every embodiment of the subject matter in separate patents. Thus, this requirement for Election of Species would be improper because an embodiment of a general method or process is not distinct from the general method or process which, as claimed, does not depend on particular "species". Further, there would be no burden on the Office to search and examine "species" of *in vitro*, *ex vivo* or *in vivo* introduction of the nucleic acid into cells or of carrying out the selective proliferation *in vivo* vs. *in vitro* unless ~~and until it is determined that the general method of providing for selective~~ proliferation of a first cell relative to a second cell is *per se* unpatentable. The Examiner would perform the same search irrespective of these "species", and this search would be directed to a method of providing for selective proliferation of a first cell relative to a second cell in which a nucleic acid is introduced into the first cell such that it confers on the first cell a resistance to conditions that inhibit the growth (viability and/or proliferation) of the second cell.

Similarly, an Election of Species in the Group 4 claims of the Restriction Requirement as redrawn above would be improper because *in vivo* vs. *ex vivo* introduction of the heterologous nucleic acid into a first cell are embodiments of a general method for trasferring heterologous nucleic acids into an organism by selective proliferation and/or viability of a first cell in the organism that contains the heterologous nucleic acid and a marker nucleic acid, relative to a similar cell in the organism that does not contain the marker nucleic acid.

4) The Restriction Requirement may result in extended patent coverage for claims directed to the same underlying principle because obviousness-type double-patenting cannot be asserted between patents containing claims belonging to different restricted groups

Furthermore, with the Requirement as set forth, Applicant could ultimately obtain a multitude of patents, each to one of the groups, that expire on different days. Since the Office has determined that claims based on nucleic acids encoding different enzymes, or selective proliferation being carried out *in*

vivo vs. in vitro, or nucleic acids being introduced into cells *in vivo*, *ex vivo* or *in vitro* are restrictable as distinct "inventions", multiple patents could issue. Obviousness-type double patenting could not be asserted in this situation, and a later-issuing patent could possibly extend patent coverage. See MPEP 806, paragraph 3, which states:

> [w]here inventions are related as disclosed but are not distinct as claimed, restriction is never proper. Since, if restriction is required by the Office double patenting cannot be held, it is imperative the requirement should never be made where related inventions as claimed are not distinct.

See, also MPEP 804.01, which states:

> 35 U.S.C.121, third sentence, provides that wherein the Office requires restriction, the patent of either the parent or any divisional application thereof conforming to the requirement cannot be used as a reference against the other. This apparent nullification of double patenting as ground of rejection or invalidity in such cases imposes a heavy burden on the Office to guard against erroneous requirements for restriction where the claims define essentially the same inventions in different language and which, if acquiesced in, might result in the issuance of several patents for the same invention.

Thus, obviousness-type double patenting cannot be asserted between a claim that recites:

> A method of providing for selective proliferation, viability or proliferation and viability of a first cell relative to a second cell, comprising:
>
> introducing a nucleic acid encoding altered mammalian inosine monophosphate dehydrogenase (IMPDH) into the first cell; and
>
> exposing the first and second cells to conditions that inhibit unaltered mammalian IMPDH but to which the altered IMPDH enzyme is resistant;
>
> whereby the first cell exhibits greater proliferation, viability or proliferation and viability relative to the second cell.

and a claim that recites:

> A method of providing for selective proliferation, viability or proliferation and viability of a first cell relative to a second cell, comprising:

introducing a nucleic acid encoding altered ribose phosphate pyrophosphokinase into the first cell; and

exposing the first and second cells to conditions that inhibit unaltered ribose phosphate pyrophosphokinase but to which the altered ribose phosphate pyrophosphokinase enzyme is resistant;

whereby the first cell exhibits greater proliferation, viability or proliferation and viability relative to the second cell.

In both the above methods of selective proliferation, the same steps are carried out to render a first cell selectively more viable and/or proliferative relative to a second cell. Both method claims have a step that involves ~~introducing a nucleic acid encoding an altered form of an enzyme into a first cell~~ such that the nucleic acid-encoded enzyme confers resistance on the first cell relative to a second cell under conditions that inhibit the unaltered form of the enzyme. The difference is in the choice of the altered enzyme to be used, not the steps of the method. Yet, two different patents claiming the above two methods could issue in this case that would extend patent coverage for the above method because obviousness-type double patenting could not be asserted in this situation.

Similarly, obviousness-type double patenting cannot be asserted between a claim that recites:

A method of providing for selective proliferation, viability or proliferation and viability of a first cell relative to a second cell, comprising:

introducing a nucleic acid encoding altered mammalian inosine monophosphate dehydrogenase (IMPDH) into the first cell *in vitro*; and

exposing the first and second cells to conditions that inhibit unaltered mammalian IMPDH but to which the altered IMPDH enzyme is resistant;

whereby the first cell exhibits greater proliferation, viability or proliferation and viability relative to the second cell.

and a claim that recites:

A method of providing for selective proliferation, viability or proliferation and viability of a first cell relative to a second cell, comprising:

introducing a nucleic acid encoding altered mammalian inosine monophosphate dehydrogenase (IMPDH) into the first cell *in vivo* in an organism; and

exposing the first and second cells to conditions that inhibit unaltered IMPDH but to which the altered IMPDH enzyme is resistant;

whereby the first cell exhibits greater proliferation, viability or proliferation and viability relative to the second cell.

In both the above methods of selective proliferation, the same steps are carried out to render a first cell selectively more viable and/or proliferative relative to a second cell. The difference lies in whether the nucleic acid encoding the altered IMPDH enzyme is introduced into the cell *in vitro* or *in vivo*. The claims are not to methods of introducing nucleic acids into cells, but to a method of selective proliferation. Yet, two different patents claiming the above two methods could issue in this case.

B) No Burden on the Office

As discussed above, the subject matter as divided by the Office is not independent or distinct. In addition, it is respectfully submitted that the Office has failed to demonstrate that there is a serious burden necessitating such extensive restriction (see MPEP 803.02; 806.04(a)).

Applicant is entitled to have a plurality of claims of differing scope in an application examined. In this instance there are 165 claims and a 130-way (including the requirement for election of a single sequene of nucleotides) restriction requirement. This application does not warrant nor support 130 different patents.

Applicant is entitled to claim the subject matter under one or more claims of varying scope. Under U.S. patent practice, an Applicant is not required to claim each and every embodiment of the subject matter they wish to protect as separate single claimed embodiments and in different patents. Thus, this restriction is improper.

Also, the fact that subject matter has different primary classifications is evidentiary of a burden, but not conclusive and is not demonstrative of a serious

burden. The mandatory search for each of the groups is, if not identical, substantially coincident. For example, the Office has indicated that (A) Groups II-IV, VI-XX, XXII, XXIV and XXVI have been identified as having claimed subject matter classified in Class 514, subclass 44; (B) that Groups V, XXI, XXIII and XXV have been identified as having claimed subject matter classified in Class 424, subclass 93.21; and (C) Group I has been identified as having claimed subject matter classified in Class 435, subclass 183. The Examiner is under no burden to search disparate classes/subclasses within any collection of Groups in (A) and (B). Thus, there is no undue burden on the Office to search and examine the claimed subject matter.

TRAVERSAL OF SEQUENCE ELECTION REQUIREMENT

The Examiner alleges that each of the twenty-six groups as restricted above reads on patentably distinct sequences, and requires Applicant to elect a single amino acid sequence for an elected Group drawn to amino acid sequences, or a single nucleic acid sequence for an elected Group drawn to nucleotide sequences. It is asserted that "the multitude of sequence submissions for examination has resulted in an undue search burden if more than one nucleic acid sequence is elected, thus making the previous waiver for up to 10 nucleic acid sequences effectively impossible to reasonably implement."

Applicant respectfully submits that the Sequence Election Requirement is improper. Although only Group III is elected with traverse in the instant application, traversal of the Sequence Election Requirement with respect to all twenty-six groups is made in the interest of further divisional applications in which claims belonging to the non-elected groups may be filed.

Restrictions to single nucleotide sequences are discussed in §803.04 of the Manual of Patent Examining Procedure (MPEP). According to MPEP §803.04, claims drawn to nucleotide sequences encoding different proteins are deemed properly restrictable, although the Commissioner has decided *sua*

sponte to partially waive this requirement for a reasonable number (usually, ten) of patentably distinct sequences. MPEP §803.04 states:

> Accordingly, in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction. In addition to the specifically selected sequences, those sequences which are patentably indistinct from the selected sequences will also be examined. Furthermore, nucleotide sequences encoding the same protein are not considered to be independent and distinct inventions and will continue to be examined together.

~~Groups I and II~~

The Group I claims are directed to an isolated altered human IMPDH protein containing one or more alterations in a specified sequence of amino acids (amino acids 330-451) within the IMPDH sequence represented by SEQ ID NO. 2. Group II claims are directed to an isolated nucleic acid molecule encoding the altered IMPDH protein of Group I.

Thus, contrary to the Examiner's assertion, there is not a "multitude" of sequences submitted for examination by these claims. Only discrete, specific alterations within a single gene sequence are claimed.

The Examiner nevertheless asserts that even submissions of 2-10 sequences constitutes an undue search burden due to the multitude of sequence submissions received at the Patent Office, thus making the previous waiver for a small number od sequences (up to 10) effectively impossible to reasonably implement. As noted above, however, MPEP §803.04 describes "independent and distinct" nucleic acid sequences subject to restriction as sequences encoding different proteins. In fact, MPEP §803.04 explicitly notes that "nucleotide sequences encoding the same protein are not considered to be independent and distinct inventions and will continue to be examined together." (emphasis added). The claims of Groups I and II are drawn to a single protein, namely, IMPDH. Therefore, the sequences claimed in each of these two groups do not constitute independent and distinct, restrictable subject matter.

Thus, the Sequence Election Requirement as applied to Groups I and II is improper not only because there is not a "multitude" of sequences submitted for examination by these claims, but also because the sequences claimed in each of these groups are not independent and distinct "inventions" as to be restrictable to begin with.

Groups III-XXVI

It is respectfully submitted that the patentability of the claims of groups III-XXVI do not require the particulars of a sequence of nucleic acid or protein; ~~each is patentable and searchable without selection of sequences.~~

First, Applicant respectfully notes that the claims of Groups III-XXVI are drawn to methods, not sequences. According to MPEP §803.04, the restriction of sequences applies to "applications claiming more than ten [usually] individual independent and distinct nucleotide sequences" (emphasis added). The claims of Groups III-XXVI are method claims and do not claim sequences; they are therefore not subject to a Sequence Election Requirement.

Second, the generic concept set forth in the instant application is not directed to particular nucleic acid or protein sequences. For example, Claim 23 is directed to a method "of providing for selective proliferation, viability or proliferation and viability of a first cell relative to a second cell," comprising:

> introducing a nucleic acid encoding an altered mammalian enzyme into the first cell; and
>
> exposing the first and second cells to conditions that inhibit the unaltered mammalian enzyme but to which the altered mammalian enzyme is resistant;
>
> whereby the first cell exhibits greater proliferation, viability or proliferation and viability relative to the second cell.

Thus, Claim 23 is a generic method claim that provides for selective proliferation of a first cell relative to a second cell based on the underlying principle that such selective proliferation can be achieved by introducing a nucleic acid encoding an altered enzyme into the first cell such that the altered

enzyme confers resistance on the first cell to conditions to which both the first and second cells are exposed. Enzymes such as IMPDH, DHODH and others recited in the claims are only exemplary of the types of enzymes that may be altered to achieve the generic principle of selective proliferation as claimed. The generic principle of selective proliferation is not limited to any particular nucleic acid or protein sequence.

Further, a search of the generic method of selective proliferation as instantly claimed is not based on a search of particular protein or nucleic acid ~~sequences. A search for selective proliferation that is achieved as a result of~~ carrying out the combination of steps as set forth in the generic method would necessarily include <u>any</u> nucleic acid encoding an altered or otherwise resistant enzyme that is introduced into a first cell and not into a second cell. By requiring restriction to a single sequence, the Requirement for Restriction, without citing any art, is urging that a method of selective proliferation as claimed is not patentable unless it is drawn to a particular nucleic acid or protein sequence. The Requirement for Restriction provides no evidence of record that the claimed method of selective proliferation is only patentable as to particular sequences, nor are there any other reasons set forth for requiring restriction of the generic claims to particular nucleic acid or protein sequences.

The claimed methods of selective proliferation or of introducing heterologous nucleic acids into cells using selective proliferation are comparable to other generic methods. Just like any other generic method, such as a method for sequencing (see, U.S. Patent No. 5,547, 835, 5,580,733 and 5,003,059), or method for detecting a target (U.S. Patent No. 5,605,798) the method should not be limited to the particular nucleic acid molecules sequenced or detected. By requiring restriction to a single nucleic acid or protein sequence, the Office, without citing any art, is urging that the generic method as claimed is not patentable. There is no evidence of record that the patentability of the method depends upon the nucleic acid introduced into the first cell, or on the

altered enzyme encoded by it. Therefore, restriction to single nucleic acid or protein sequences in the method claims of Groups III-XXVI is improper.

Furthermore, restriction and election of species also requires the Office to establish that there is a burden on the Office to examine the species or groups in a single application. In this instance, as discussed above, since the method is searchable without reference to particular nucleic acid molecules, there is no burden on the Office to examine the method claims of Groups III-XXVI on the merits without a further sequence election requirement.

SUMMARY

For the reasons provided above, Applicant respectfully requests reconsideration and removal of the Restriction Requirement as between Groups III-XXVI. Further, Applicant respectfully requests reconsideration and removal of the Sequence Election Requirement as to all twenty-six groups.

* * *

In view of the above, examination of the application on the merits is respectfully requested.

Respectfully submitted,
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Michael C. Jensen

Serial No. 09/846,637
Conf. No. 4845

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For: Selection Systems for Genetically Modified Cells

Art Unit: 1632

Examiner: Chen, Liping

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Arlington, VA 22202

Jonathan Ong

MARKED UP CLAIMS (37 CFR §1.121)

Please amend claims 150 and 159 as follows:

150. (Amended) The method of claim [137] 138, wherein the heterologous nucleic acid molecule encodes a product that alters the organism's immune responses and the conditions comprise administering to the organism an immunosuppressive agent.

159. (Amended) The method of claim [130] 131, wherein the organism has undergone a bone marrow or solid organ transplantation.